



UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

NOTICE OF ALLOWANCE AND ISSUE FEE DUE

HM31/0923

ROBERT S MACWRIGHT
SKADDEN ARPS SLATE MEAGHER & FLOW
919 THIRD AVENUE
NEW YORK NY 10022

| APPLICATION NO. | FILING DATE | TOTAL CLAIMS | EXAMINER AND GROUP ART UNIT | DATE MAILED |
|-----------------------|-------------------------|--------------|-----------------------------|---------------|
| 08/727,509 | 10/22/96 | 020 | SIEM, J | 1634 09/24/98 |
| First Named Applicant | DARZYNKIENICZ, ZBIGNIEW | | | |

TITLE OF INVENTION METHODS FOR LABELING DNA ENDS WITH HALOGENATED NUCLEOTIDES AND DETECTING SAME WITH ANTIBODIES

| ATTY'S DOCKET NO. | CLASS-SUBCLASS | BATCH NO. | APPLN. TYPE | SMALL ENTITY | FEE DUE | DATE DUE |
|-------------------|----------------|-----------|-------------|--------------|----------|----------|
| 1 1075-PCT. | 435-006.000 | J45 | UTILITY | YES | \$660.00 | 12/24/98 |

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED.

THE ISSUE FEE MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED.

HOW TO RESPOND TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is changed, pay twice the amount of the FEE DUE shown above and notify the Patent and Trademark Office of the change in status, or

B. If the status is the same, pay the FEE DUE shown above.

If the SMALL ENTITY is shown as NO:

A. Pay FEE DUE shown above, or

B. File verified statement of Small Entity Status before, or with, payment of 1/2 the FEE DUE shown above.

II. Part B-Issue Fee Transmittal should be completed and returned to the Patent and Trademark Office (PTO) with your ISSUE FEE. Even if the ISSUE FEE has already been paid by charge to deposit account, Part B Issue Fee Transmittal should be completed and returned. If you are charging the ISSUE FEE to your deposit account, section "4b" of Part B-Issue Fee Transmittal should be completed and an extra copy of the form should be submitted.

III. All communications regarding this application must give application number and batch number.

Please direct all communications prior to issuance to Box ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PATENT AND TRADEMARK OFFICE COPY

Notice of Allowability

Application No.
08/727,509

Applicant(s)
Darzynkiewicz, Zbigniew

Examiner
Jeffrey Siew

Group Art Unit
1634



All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance and Issue Fee Due or other appropriate communication will be mailed in due course.

☒ This communication is responsive to response filed 9/3/98

#12

☒ The allowed claim(s) is/are 1-20

☐ The drawings filed on _____ are acceptable.

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

A SHORTENED STATUTORY PERIOD FOR RESPONSE to comply with the requirements noted below is set to EXPIRE **THREE MONTHS** FROM THE "DATE MAILED" of this Office action. Failure to timely comply will result in ABANDONMENT of this application. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

☐ Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL APPLICATION, PTO-152, which discloses that the oath or declaration is deficient. A SUBSTITUTE OATH OR DECLARATION IS REQUIRED.

☒ Applicant MUST submit NEW FORMAL DRAWINGS

☐ because the originally filed drawings were declared by applicant to be informal.

☒ including changes required by the Notice of Draftsperson's Patent Drawing Review, PTO-948, attached hereto or to Paper No. 5

☐ including changes required by the proposed drawing correction filed on _____, which has been approved by the examiner.

☐ including changes required by the attached Examiner's Amendment/Comment.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the reverse side of the drawings. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

☐ Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Any response to this letter should include, in the upper right hand corner, the APPLICATION NUMBER (SERIES CODE/SERIAL NUMBER). If applicant has received a Notice of Allowance and Issue Fee Due, the ISSUE BATCH NUMBER and DATE of the NOTICE OF ALLOWANCE should also be included.

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

☐ Interview Summary, PTO-413

☐ Examiner's Amendment/Comment

☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material

☒ Examiner's Statement of Reasons for Allowance

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REASONS FOR ALLOWANCE

1. The following is an examiner's statement of reasons for allowance:

No prior art has been found teaching or suggesting the labeling of ends of nuclear DNA within cells by enzymatically end labeling with halogenated deoxynucleotide triphosphate and reacting with labeled anti halogenated deoxynucleotide antibody which specifically binds to the halogenated nucleotide.

The closest art is Gorczyca et al (Cancer Research 53 pp. 1945-1952 , April 15, 1993), Vanderlaan et al (US 5,053,336 October 1, 1991 and Xun Li et al (Int. J. Of Oncology.vol. 4, pp 1157-1161, 1994).

Gorczyca et al teach the detection of DNA strand breaks in apoptotic cells. Using terminal deoxynucleotidyl transferase (TdT), the ends of nuclear DNA strand breaks were labeled with biotinylated dUTP in apoptotic cells and subsequently detected in situ with labeled antibodies (see page 1, line 3 abstract).

Vanderlaan et al. teach the detection of halogenated nucleotides that were bound during normal DNA synthesis, using monoclonal antibodies specific to these halogenated nucleotides (see column 9, line 40) .

Xun Li et al. teach the use of 5-bromo-2-deoxyuridine for the photolysis of DNA and that the breakage of DNA strands can be detected by biotin labeled nucleotides, catalyzed by TdT.

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The strand breaks of the DNA were generated by photolysis and eliminated the denaturation step (see page 1158, Materials and Methods).

2. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."
3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Siew whose telephone number is (703) 305-3886 and whose e-mail address is jsiew@uspto.gov. The examiner can normally be reached on Monday through Friday from 6:30 a.m. to 3 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist for Technology Center 1600 whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette,

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1096 OG 30 (November 15, 1989). The CM1 Center numbers for Group 1600 are Voice (703).

308-3290 and Fax (703) 305-3014 or (703) 305-4242.

J. Seew
9/22/98

KENNETH R. HORLICK
PRIMARY EXAMINER
GROUP ~~1000~~ 1600 9/22/98
Kenneth R. Horlick, Ph.D.